

---

**Type 2 innate signals stimulate fibro/adipogenic progenitors to facilitate muscle regeneration.**

<b>Journal:</b>	Cell
<b>Publication Year:</b>	2013
<b>Authors:</b>	Jose E Heredia, Lata Mukundan, Francis M Chen, Alisa A Mueller, Rahul C Deo, Richard M Locksley, Thomas A Rando, Ajay Chawla
<b>PubMed link:</b>	23582327
<b>Funding Grants:</b>	Stanford CIRM Training Program

**Public Summary:**

A rapid response to injury by the immune system is a hallmark of the regenerative process in muscle. Although this response is thought to be crucial for healthy tissue recovery, the mechanisms that govern the crosstalk between the immune cells and stem cells of muscle are an area of active investigation. We show that a subset called the type 2 innate immune response is important for regeneration. In particular, immune cells release a molecule called IL-4 that support the function of a resident population of fibroadipogenic progenitors. These progenitors, in turn, send signals to muscle stem cells that allow them to properly divide and repair muscle fibers.

**Scientific Abstract:**

In vertebrates, activation of innate immunity is an early response to injury, implicating it in the regenerative process. However, the mechanisms by which innate signals might regulate stem cell functionality are unknown. Here, we demonstrate that type 2 innate immunity is required for regeneration of skeletal muscle after injury. Muscle damage results in rapid recruitment of eosinophils, which secrete IL-4 to activate the regenerative actions of muscle resident fibro/adipocyte progenitors (FAPs). In FAPs, IL-4/IL-13 signaling serves as a key switch to control their fate and functions. Activation of IL-4/IL-13 signaling promotes proliferation of FAPs to support myogenesis while inhibiting their differentiation into adipocytes. Surprisingly, type 2 cytokine signaling is also required in FAPs, but not in myeloid cells, for rapid clearance of necrotic debris, a process that is necessary for timely and complete regeneration of tissues.

---

**Source URL:** <https://www.cirm.ca.gov/about-cirm/publications/type-2-innate-signals-stimulate-fibroadipogenic-progenitors-facilitate>